

REMARKS

At page 3 of the Office Action of February 12, 2003, several objections are made. These objections are rendered moot by the amendments to the claims as indicated above. Specifically, claim 6 as amended is directed to polynucleotides that encode SEQ ID NO:6, wherein the amino acid at position 231 is Alanine, and claims 7 and 8 have been canceled.

Rejection under 35 U.S.C. §112, first paragraph, written description:

The claims are rejected as lacking sufficient written description in the specification. Claims 7 and 8 are specifically mentioned in the office action, however, Applicant notes that the arguments presented herein are applicable to all pending claims.

Claim 6 as amended is directed to nucleotide sequences that encode the amino acid sequence as set forth in SEQ ID NO:6. Thus, as the genetic code is widely known and understood, the skilled artisan could, without undue experimentation, identify or make any polynucleotide encompassed by the claims. As examples of such nucleotide sequences are described in the specification, it is apparent that the inventors had possession of the claimed invention at the time of filing.

Rejection under 35 U.S.C. §112, first paragraph, scope:

Claims 6-9, and 11-15 are rejected as lacking enabling disclosure in the specification. Specifically, the Office emphasizes that the examples show *in vitro* transfection, and that such data cannot be extrapolated to cover *in vivo* embodiments.

The claims, as amended, are directed to polynucleotides. Those polynucleotides are described as encoding SEQ ID NO:6, and being capable of inhibiting endothelial cell proliferation *in vitro*. The examples provide guidance on assaying the polynucleotides for the ability to inhibit endothelial cell proliferation *in vitro*. Since the claims are directed to a composition that is defined extensively in terms of its structure, and the functional limitation is directed to *in vitro* assays, the arguments put forth by the Office regarding extrapolation of *in vitro* data to the *in vivo* environment are not applicable. Since

Applicant has shown examples of polynucleotides that are within the scope of the structural definition of the claims, and since Applicant has shown that these polynucleotides possess the ability to inhibit endothelial cell proliferation in vitro, the scope of the claims is commensurate with the teachings of the specification, and therefore, the claims meet the enablement requirement.

Rejection under 35 U.S.C. §102:

Claims 6-9 are rejected under 35 U.S.C. §102 as being anticipated by Griffith et al. The Office cites Griffith as teaching construction of a polynucleotide encoding a MetAP2 H231A variant, and that such mutation results in complete loss of catalytic activity.

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Applicant first notes that the cited reference does not teach a MetAP2 H231A variant. The only mention of such a mutation is in the figure legend of figure 5. In the attached declaration under 37 C.F.R. §1.132 of Yie-Hwa Chang, Ph.D., a co-author of the cited reference, states that the reference to H231A in that figure legend is incorrect. The mutation actually constructed was H231N. In addition, throughout the text of the reference H231N is consistently described, as well as in the lane markers for figure 5B. It would have been apparent to anyone reading that reference that the mention of H231A in the figure legend for figure 5 is erroneous, based on the consistent reference to H231N throughout the rest of the reference. Such a typographical error does not adequately teach the H231A mutation. *In re Yale*, 434 F2d 666 (CCPA 1970). Further, a skilled artisan would have immediately recognized the reference to H231A as a typographical error, as supported by the declaration of Yie-Hwa Chang at paragraph 4. In addition, the skilled artisan would not have been motivated to construct the H231A variant due to protein conformation considerations due to the non-conservative nature of that substitution, as supported by the declaration of Yie-Hwa Chang at paragraph 6.

Further, the Office contends that Griffith et al. teaches that the H231N mutation results in complete loss of catalytic activity. Applicant points out that the claimed polynucleotides have dominant negative MetAP2 activity, i.e., the claimed polynucleotides inhibit endothelial cell proliferation in vitro. Griffith et al. does not teach

or suggest such activity. Therefore, the claimed polynucleotides cannot be anticipated by the teachings of Griffith et al.

Rejection under 35 U.S.C. §103:

Claims 11-15 are rejected as being obvious over Griffith et al., in view of U.S. patent no. 6,110,744. Griffith et al. is cited as above. U.S. patent no. 6,110,744 is cited as teaching an adenovirus vector comprising a heterologous gene and a promoter which is CMV.

Applicant respectfully points out that Griffith et al. do not teach a MetAP2 H231A variant, as discussed above and in the declaration of Yie-Hwa Chang, Ph.D. Therefore, Griffith et al. in view of U.S. patent no. 6,110,744 cannot render the instant claims obvious.

Conclusion:

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, he is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,



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